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Canine Heartworm Treatment: A Team Approach to Adulticide Therapy

Although varying treatment protocols exist for canine heartworm (*Dirofilaria immitis*) disease, the 3-dose injection protocol with an adulticide such as Immiticide® (melarsomine dihydrochloride), as described by the American Heartworm Society, is considered a safe and effective treatment for most dogs with heartworm disease.¹

Setting Clients Up for Success

Because of the inherent risks involved with heartworm treatment, many clients are fearful and will need support from the veterinary team. All team members can help by communicating the following:

- Clients are not alone, and the veterinary team will support them throughout the entire process.
- Restricting their dog's activity throughout (and beyond) treatment is imperative, but acknowledge that it may be difficult.
 - Provide resources on how to keep their dog mentally stimulated without physical exercise.²
 - Some dogs may benefit from anti-anxiety supplements or drugs.
- Dogs may experience transient anxiety and discomfort after Immiticide® treatment. Pain medication can be prescribed to control discomfort.
- Clients should monitor their dog closely through the several-month

treatment process. They should be cautioned to seek emergency care if signs of respiratory distress, coughing up blood, or lethargy are seen.

- Clients will need to keep their dog on heartworm prevention long-term to prevent reinfection.¹

Pearls of Treatment

Heartworm-infected dogs will be started or continued on monthly heartworm prevention at the time of diagnosis, which will affect immature worms and prevent new infection.¹ Dogs with high microfilaria burdens may experience reactions; consistent monitoring after administration of the first dose is recommended.¹ High-risk dogs should be pretreated with antihistamines and corticosteroids.¹ Exercise restriction should begin at the time of diagnosis.¹

All dogs should receive doxycycline, an antibiotic, for 1 month prior to administration of Immiticide® injection to kill *Wolbachia* spp bacteria found in heartworms.¹ This will reduce the inflammation and risk associated with adulticide therapy.¹ Following the AHS timeline, the 3-dose protocol with Immiticide® will begin and, once completed, will eliminate ≈98% of adult heartworms in the dog's body.¹ For a step-by-step guide on the 3-dose injection protocol, visit the AHS website.¹

Pulmonary thromboembolism caused by dying adult heartworms is a risk of

Immiticide® treatment.¹ Tapering corticosteroid doses can help reduce severity in most cases.¹ Dogs with more severe signs are at increased risk. It should be emphasized to owners that reducing their dog's activity level is one of the most critical factors in avoiding serious complications and having a successful treatment outcome.

Dogs are considered heartworm-free once 2 negative antigen tests are achieved 6 months apart.¹ The 3-dose protocol does not guarantee elimination of heartworm infection, which is why continued testing is important.

Conclusion

The best possible experience and outcome for both the patient and the client can be achieved by educating the entire veterinary team about the heartworm treatment process. Given the inherent risks of treatment, having open lines of communication between the veterinarian, veterinary team, and client can help lead to more successful outcomes.

Share this handout with your team!
Download and access the references
at [cliniciansbrief.com/
article/team-approach-
adulticide-therapy](https://www.cliniciansbrief.com/article/team-approach-adulticide-therapy).



IMPORTANT SAFETY INFORMATION

IMMITICIDE Sterile Powder should not be used in dogs with very severe (Class 4) heartworm disease. **IMMITICIDE Sterile Powder should be administered by deep intramuscular injection in the lumbar (epaxial) muscles (L3–L5) only. Do not use in any other muscle group. Do not use intravenously. Care should be taken to avoid superficial injection or leakage.** Serious adverse reactions may occur in any dog with heartworm disease due to the killing of heartworms in the pulmonary arteries. Reactions may include thromboembolism, dyspnea, coughing, depression, right side heart failure, and death. Dogs should be cage rested following treatment due to possible thromboembolic disease. Post-injection site reactions (eg, pain, swelling) were the most commonly reported adverse events. See full prescribing information for dosing and administration directions prior to each use of IMMITICIDE Sterile Powder. For full prescribing information, visit [IMMITICIDEclinic.com](https://www.immiticideclinic.com).

IMMITICIDE[®] Sterile Powder (melarsomine dihydrochloride)

Approved by FDA under NADA # 141-042

CAUTION

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

WARNING

IMMITICIDE[®] should be administered by deep intramuscular injection in the lumbar (epaxial) muscles (L3 - L5) ONLY. DO NOT USE IN ANY OTHER MUSCLE GROUP. DO NOT USE INTRAVENOUSLY. Care should be taken to avoid superficial injection or leakage. (See SAFETY).

ACTIVE INGREDIENT

IMMITICIDE Sterile Powder contains 50.0 mg melarsomine dihydrochloride and 33.75 mg glycine USP. 1 vial: when reconstituted with the provided 2 mL of STERILE DILUENT (sterile water for injection) contains 25 mg/mL of active ingredient.

PHARMACOLOGY

Melarsomine dihydrochloride is an organic arsenical chemotherapeutic agent. Melarsomine has a molecular weight of 501.34 and is chemically designated as 4 - [(4, 6-diamino-1, 3, 5- triazon-2-yl) amino] phenyl-dithioarsenite of di (2-aminoethyl), dihydrochloride. It is freely soluble in water. When injected intramuscularly, it is rapidly absorbed. The exact mode of action on *D. immitis* is unknown.

INDICATIONS

IMMITICIDE Sterile Powder is indicated for the treatment of stabilized Class 1^a, 2^b, and 3^c heartworm disease caused by immature (4 month-old, stage L₃) to mature adult infections of *Dirofilaria immitis* in dogs.

Heartworm Disease Classification: The following parameters were used to classify the dogs in the clinical field trials for IMMITICIDE. Other parameters may be considered. As a general rule, conservative treatment should be employed since heartworm disease is serious and potentially fatal. If there is evidence of a high worm burden, patients should be categorized as Class 3.

^a Class 1: Patients in this category are characterized as having asymptomatic to mild heartworm disease. No radiographic signs or signs of anemia are evident. Patients with mild disease may have subjective signs such as a general loss of condition, fatigue on exercise, or occasional cough; however, no objective radiographic or other abnormal laboratory parameters will be present.

^b Class 2: Patients in this category are characterized as having moderate heartworm disease. Radiographic signs or signs of anemia [Packed Cell Volume (PCV) less than 30% but greater than 20%, or other hematologic parameters below normal] are evident. Mild proteinuria (2+) may be present. Radiographic signs may include right ventricular enlargement, slight pulmonary artery enlargement, or circumscribed perivascular densities plus mixed alveolar/interstitial lesions. Patients may be free of subjective clinical signs or may have a general loss of condition, fatigue on exercise, or occasional cough. If necessary, patients should be stabilized prior to treatment.

^c Class 3: Patients in this category are characterized as having severe heartworm disease. These patients have a guarded prognosis. Subjective signs of disease may include cardiac cachexia (wasting), constant fatigue, persistent cough, dyspnea, or other signs associated with right heart failure such as ascites and/or jugular pulse. Radiographic signs may include right ventricular enlargement or right ventricular plus right atrial enlargement, severe pulmonary artery enlargement, circumscribed to chronic mixed patterns and diffuse patterns of pulmonary densities or radiographic signs of thromboembolism. Signs of significant anemia (PCV <20% or other hematologic abnormalities) may be present. Proteinuria (> 2+) may be present. Patients may have only moderate clinical signs and significant laboratory or radiographic alterations or they may have significant clinical signs with only moderate laboratory and radiographic signs and be categorized as Class 3. Patients in Class 3 should be stabilized prior to treatment and then administered the alternate dosing regime (See **PRECAUTIONS** and **DOSAGE AND ADMINISTRATION**).

CONTRAINDICATIONS

IMMITICIDE is contraindicated in dogs with very severe (Class 4) heartworm disease. Patients in this category have Caval Syndrome (*D. immitis* present in the venae cavae and right atrium).

WARNINGS

(See **boxed Warning**). For use in dogs only. Safety for use in breeding animals and lactating or pregnant bitches has not been determined.

HUMAN WARNINGS

Keep this and all medications out of the reach of children. Avoid human exposure. Wash hands thoroughly after use or wear gloves. Potentially irritating to eyes. Rinse eyes with copious amounts of water if exposed. Consult a physician in cases of accidental exposure by any route (dermal, oral or by injection).

The Safety Data Sheet (SDS) contains more detailed occupational safety information.

To report adverse effects, obtain an SDS or for assistance, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251.

PRECAUTIONS

General: All dogs, with heartworm disease are at risk for post-treatment pulmonary thromboembolism (death of worms which may result in fever, weakness, and coughing), though dogs with severe pulmonary arterial disease have an increased risk and may exhibit more severe signs (dyspnea, hemoptysis, right heart failure and possibly death). Dogs should be restricted from light to heavy exercise post-treatment depending on the severity of their heartworm disease.

Studies in healthy (heartworm negative) dogs indicate that adverse reactions may occur after the second injection in the series even if no problems were encountered with the first injection. All patients should be closely monitored during treatment and for up to 24 hours after the last injection.

Special Considerations for Class 3 dogs: Following stabilization, severely ill (Class 3) dogs should be treated according to the alternate dosing regime in an attempt to decrease post-treatment mortality associated with thromboembolism (See **DOSAGE AND ADMINISTRATION**). Post-treatment mortality due to thromboembolism, and/or progression of the underlying disease may occur in 10 to 20% of the Class 3 patients treated with IMMITICIDE (see **Mortality**). Hospitalization post-treatment and strict exercise restriction are recommended. Other supportive therapies should be considered on a case-by-case basis.

If the alternate dosing regime is used, expect increased injection site reactions on the side receiving the second injection since the skeletal muscles at the first injection site may not have fully recovered (healed). If persistent swelling is present at 1 month, the second injections may be delayed for several weeks up to 1 month.

Special Considerations for Older Dogs: In clinical field trials, dogs 8 years or older experienced more post-treatment depression/lethargy, anorexia/inappetence, and vomiting than younger dogs.

SAFETY

IMMITICIDE has a low margin of safety. A single dose of 7.5 mg/kg (3X the recommended dose) can result in pulmonary inflammation, edema, and death. Daily administration of 2X and 3X the recommended dose for 6 days caused no renal injury; however, daily administration of these doses for 14 days caused renal damage in healthy dogs. Adverse reactions, primarily at the injection sites, were seen at the recommended dose in clinical trials (see **ADVERSE REACTIONS**).

Studies in Healthy (Heartworm Negative) Dogs: The safety of IMMITICIDE was studied in 24 healthy beagle dogs. Drug was administered at 0, 2.5, 5.0 and 7.5 mg/kg for 6 consecutive days (0, 1, 2 and 3 times the recommended dosage). Clinical observations included tremors, lethargy, unsteadiness/ataxia, restlessness, panting, shallow and labored respiration, and/or rales. These signs were seen in all groups treated with IMMITICIDE with frequency and intensity increasing with increasing dosage. Death or euthanasia in a moribund state occurred in 3/6 dogs in the 7.5 mg/kg (3X) group. The signs exhibited by these dogs, in addition to the signs described above, included collapse, severe salivation, vomiting, respiratory distress, cyanosis, stupor, and death within 4 hours of the first dose in two dogs and within 20 hours of the second dose in one dog.

Body weights, water consumption, hematology and urine parameters were comparable to controls. Decreased food consumption occurred sporadically in the two high dose groups. Elevations, up to 25-fold, in creatinine kinase (CK) and elevations, up to 7-fold, in aspartate aminotransferase (AST) were observed and related grossly and histologically to muscle damage at the injection sites. Up to 2-fold elevations in alanine aminotransferase (ALT) were also noted. Gross and microscopic pathology revealed no organ-related toxicity other than edema and acute inflammation in the lungs and pleural effusion in the 3 dogs that died at the 7.5 mg/kg dose. Injection site irritation was observed in the skeletal muscles at all dose levels. At 5.0 mg/kg an injection site abscess was observed in one dog.

A separate study was conducted to examine the intensity and duration of injection site reactions. The dogs were dosed at 2.5 and 5.0 mg/kg (1X and 2X the recommended dose) twice 24 hours apart. This treatment series was repeated 4 months later. One group received the second treatment series after 1 month to mimic the alternate dosing regime. Swelling, which occurred within 7 days of injection and persisted from 1 to 72 days (average 30 days), was the most common clinical observation. A small, firm nodule in the lumbar region of one dog in the 1X group appeared during the first month of the study and persisted for 41 days. Pain at or following injection was not observed in this study. Elevations of the same magnitude as in the previous study and again related to muscle damage were observed in CK and AST within 8 hours of injection. The values approached pretest levels by 72 hours and were within the normal range established by control animals by 1 month post-injection.

Gross and microscopic evidence of injection site irritation (cellular infiltrate, fibrosis, necrosis, and hemorrhage) was still evident in the muscles 1 month post-injection in dogs at both dose levels. By 3 months post-injection, resolution (healing) was evident microscopically in the skeletal muscles at the 2.5 mg/kg dose level. One dog treated at the 2X dose had extension of treatment-related injection site inflammation into deeper tissues (i.e., abdominal cavity) as evidenced by an adhesion between the spleen and mesentery.

ADVERSE REACTIONS (Side Effects)

Injection Sites: At the recommended dosage in clinical field trials, significant irritation was observed at the intramuscular injection sites, accompanied by pain, swelling, tenderness, and reluctance to move. Approximately 30% of treated dogs experienced some kind of reaction at the injection site(s). Though injection site reactions were generally mild to moderate in severity and recovery occurred in 1 week to 1 month, severe reactions did occur (<1.0%), so care should be taken to avoid superficial or subcutaneous injection and leakage. Firm nodules can persist indefinitely.

Other Reactions: Coughing/gagging, depression/lethargy, anorexia/inappetence, fever, lung congestion, and vomiting were the most common reactions observed in dogs treated with IMMITICIDE.

Hypersalivation and panting occurred rarely in clinical trials (1.9% and 1.6%, respectively); however, these signs may occur within 30 minutes of injection and may be severe. One dog vomited after each injection of IMMITICIDE, despite pre-treatment with anti-emetics. All adverse reactions resolved with time or treatment with the exception of a limited number of injection site reactions (persistent nodules, see Table: **Average Onset Time and Duration (with Ranges) of the Most Common Reactions in Clinical Trials**) and a low number of post-treatment deaths. (See **Mortality**).

Prevalence of Clinical Observations/Adverse Reactions Reported in Clinical Field Trials: The following table enumerates adverse events that occurred in 1.5% or more of dogs with Class 1, 2 and 3 heartworm disease treated with IMMITICIDE in clinical field trials. Comparison is made with the same adverse events reported in dogs treated with placebo. Some of the following clinical observations/adverse reactions seen in dogs treated with IMMITICIDE may be directly attributable to the drug or they may be secondary to worm death and/or the underlying heartworm disease process.

Clinical Observation/ Adverse Reaction	Prevalence of Clinical Observation/Adverse Reactions Reported in Clinical Field Trials	
	IMMITICIDE % of dogs n=311	PLACEBO % of dogs n=63
Injection Site Reactions	32.8	3.2
Coughing/Gagging	22.2	14.3
Depression/Lethargy	15.4	4.8
Anorexia/Inappetence	13.2	3.2
Pyrexia (fever)	7.4	0.0
Lung Congestion/Sounds	5.5	1.6
Emesis	5.1	1.6
Diarrhea	2.6	0.0
Dyspnea	2.6	1.6
Hypersalivation	1.9	0.0
Panting	1.6	0.0
Hemoptysis	1.6	0.0

Clinical observations/adverse reactions occurring in less than 1.5% of the dogs treated with IMMITICIDE include: abdominal hemorrhage, abdominal pain, bloody stool/diarrhea, colitis, gingivitis, pancreatitis, anemia, DIC, hemoglobinemia, icterus (mucous membranes), discoloured urine, hematuria, inappropriate urination, low specific gravity, polyuria, pyuria, bronchitis, miscellaneous respiratory problem, pneumonia, tachypnea, tracheobronchitis, wheezing, alopecia, hair color and coat character change, miscellaneous skin problem, ataxia, disorientation, fatigue/tires easily, miscellaneous eye problem, weight loss, convulsion/seizure, leukocytosis, polydipsia, and restlessness.

Onset and Duration of Clinical Observations/Adverse Reactions: The following table is provided to show the average onset time post-treatment for the most common reactions and the average duration of each event, as calculated from the 311 dogs treated with IMMITICIDE in the clinical field trials.

Average Onset Time and Duration (with Ranges) of the Most Common Reactions in Clinical Trials

Clinical Observation/Adverse Reaction	Avg. Onset Time in Days (range)*	Avg. Duration in Days (range)*
Injection Site		
Swelling/Edema/Seroma	6 (0*-77)	18 (<1-210)
Pain/Discomfort/Irritation	1 (0-6)	3 (<1-30)
Inflammation/Heat		
Generalized/Local Myalgia with Tenderness and Stiffness	3 (1-8)	9 (<1-30)
Persistent (lumps, knots, nodules, masses)	22 (0-99)	47 (1-152)
Abscess (sterile and septic)	24 (10-42)	21 (5-36)
Coughing/Gagging	10 (0-103)	13 (<1-134)
Depression/Lethargy	5 (0-46)	6 (<1-48)
Anorexia/Inappetence	5 (0-63)	5 (<1-30)

*A zero indicates that the reaction first occurred on the day of treatment.

Mortality: Death is a possible sequelae of heartworm disease in dogs with or without treatment, especially in the Class 3 dogs. The following table shows the percentage of dogs that died in clinical trials with IMMITICIDE® (melsarsomine dihydrochloride) and the causes of death, if known.

Mortality in Dogs with Class 1, 2, and 3 Heartworm Disease Treated with IMMITICIDE in Clinical Field Trials		
	CLASS 1, 2 % OF DOGS n=267	CLASS 3 % OF DOGS n=44
Total Deaths Cause:	5.2	18.2
Trauma	2.3	2.3
Thromboembolism	0.0	4.6
Euthanasia (unrelated to treatment or underlying disease)	1.1	0.0
Euthanasia (related to treatment or underlying disease)	0.0	2.3
Underlying Disease	0.8	2.3
Undetermined	1.1	6.8

In one small (n=15), uncontrolled field study in severely ill (Class 3) dogs, 5 dogs died following treatment. Pulmonary thromboembolism was the cause of one death. The remaining dogs were not necropsied. All 5 dogs were in right heart failure at the time of treatment. Clinical signs seen in this study which were not seen in the larger studies include atrial fibrillation, collapse, hypothermia, and weakness.

Post Approval Experience: In addition to the aforementioned adverse reactions reported in pre-approval clinical studies, there have also been rare reports of paresis and paralysis in dogs following administration of IMMITICIDE.

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Overdosage: Three dogs were inadvertently overdosed with IMMITICIDE in the clinical field trials when the dose was calculated on a mg/lb basis rather than a mg/kg basis (2X overdosage). Within 30 minutes of injection, one dog showed excessive salivation, panting, restlessness, and fever with all signs resolving within 4 hours. Vomiting and diarrhea were seen in the second dog within 24 hours of injection. The dog vomited once and the diarrhea resolved within 24 hours. The third dog showed no systemic reaction to the overdosage. Clinical observations in healthy beagle dogs after receiving up to 3X the recommended dose included tremors, lethargy, unsteadiness/ataxia, restlessness, panting, shallow and labored respiration, rales, severe salivation, and vomiting which progressed to respiratory distress, collapse, cyanosis, stupor, and death. (See **SAFETY**).

BAL in Oil Ampules (Dimercaprol Injection, USP) [Akorn, San Clemente, California, at 1-800-223-9851] is reported in the literature to be an antidote for arsenic toxicity and was shown in one study to reduce the signs of toxicity associated with overdosage of IMMITICIDE. The efficacy of IMMITICIDE may be reduced with co-administration of BAL.

EFFICACY

Results of the laboratory and clinical field trials demonstrate that treatment with IMMITICIDE results in reduction and/or clearance of *D. immitis* infection in dogs with Class 1, 2, and 3 heartworm disease. Evaluations for efficacy were determined by post-mortem worm counts in the laboratory studies and detection of antigen in the blood and subjective clinical assessments in the clinical trials. Physical exams, assessments of clinical variables, class of heartworm disease, radiographic examinations, as well as complete blood counts, serum chemistry profiles, and urinalysis were evaluated in the field trials.

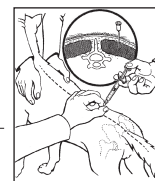
Laboratory Studies: In placebo-controlled laboratory studies, IMMITICIDE, administered at 2.5 mg/kg twice, 24 hours apart, was 90.7% effective against transplanted adult heartworms and 90.8% effective against induced infections of 4 months old (L₃) immature heartworms. To evaluate the effectiveness of the alternate dosing regimen, dogs with transplanted heartworms were treated with either 2.5 mg/kg once or 2.5 mg/kg once followed 1 month later with 2.5 mg/kg administered twice 24 hours apart. A single injection of IMMITICIDE at 2.5 mg/kg reduced male worms 87.7% and female worms 16.9% (total 51.7%). When the full regime was used 100% of male worms and 98% of female worms were killed (total 99%). Dogs with natural *D. immitis* infections were treated with IMMITICIDE at 2.5 mg/kg twice, 24 hours apart. This dose was repeated 4 months later. Antigen tests performed at month 4 showed a 90% conversion from antigen positive to negative status. Worm counts at month 9 showed a 98.7% reduction in worm numbers as compared to placebo controls.

Clinical Field Studies: In two well-controlled field studies, 169 client-owned dogs, 1 to 12 years old and weighing 3.0 to 59.0 kg, with Class 1 or stabilized Class 2 heartworm disease were treated with the recommended dose of IMMITICIDE. In-office blood antigen tests were used pre-treatment to diagnose the *D. immitis* infection and 4 months after drug administration to assess treatment response. At month 4, 76.2 to 81% of the dogs had converted from antigen positive to antigen negative status. The conversion rate ranged from 89.7 to 98.2% after two treatment series. In an open-label study in 102 dogs, 1 to 18 years old and weighing 4.4 to 40.8 kg, with Class 1 or stabilized Class 2 heartworm disease, the conversion rate was 84% 4 months after one series of treatments. When a second series was given at month 4, the conversion rate was 94%.

An open-label clinical field study was conducted in 44 dogs, 1.5 to 14 years old and weighing 3.2 to 50.0 kg, with stabilized, Class 3 heartworm disease. Dogs received the alternate dosing regime (2.5 mg/kg once followed 1 month later by 2.5 mg/kg twice 24 hours apart). The conversion rate was 89.2% 4 months after the final treatment. In a small, uncontrolled field trial (n=10) in Class 3 dogs the conversion rate was 100% 4 months after treatment.

DOSAGE AND ADMINISTRATION

IMMITICIDE should be administered ONLY by deep intramuscular injection in the epaxial (lumbar) muscles in the third through fifth lumbar region (see graphic). DO NOT ADMINISTER AT ANY OTHER SITE. Avoid superficial injection or leakage. Use a 23 gauge 1 inch needle for dogs equal to or less than 10 kg (22 lb) in weight. Use a 22 gauge 1 ½ inch needle for dogs greater than 10 kg (22 lb). Use alternating sides with each administration. If repeated administrations are warranted avoid injecting at the same lumbar location. Record the location of the first injection(s) in the patient's medical record for future reference.



Disease Classification: It is vital to classify the severity of heartworm disease to apply the appropriate dosage regime for IMMITICIDE. (See **INDICATIONS**).

Class 1 and 2:

If necessary, dogs should be stabilized prior to treatment. IMMITICIDE should be administered intramuscularly in the lumbar (L₃ - L₅) muscles at a dose of 2.5 mg/kg twice, 24 hours apart. (See **Dosing Table**). Four months following treatment, a second treatment series (2.5 mg/kg twice, 24 hours apart) can be elected taking into consideration the response to the first IMMITICIDE treatment and the condition, age, and use of the dog. Worms that were too young to be killed by the first treatment series, i.e., <4 months, may be killed by a second treatment series.

Class 3:

Alternate Dosing Regime: Dogs with severe (Class 3) heartworm disease should be stabilized prior to treatment and then dosed intramuscularly in the lumbar (L₃ - L₅) muscles with a single injection of 2.5 mg/kg then approximately 1 month later with 2.5 mg/kg administered twice 24 hours apart. (See **Dosing Table**).

Dosing Table: Care must be taken to administer the proper dose. Accurately weigh the dog and calculate the volume to be injected based on the dose of 2.5 mg/kg (1.1 mg/lb). This is equivalent to 0.1 mL/kg (0.045 mL/lb). The following table should be used as a guide to ensure that the proper volume has been calculated.

WEIGHT (LB)	2.2	4.4	6.6	8.8	11.0	13.2	15.4	17.6	19.8	22.0	44.0	66.0	88.0	110.0
WEIGHT (KG)	1	2	3	4	5	6	7	8	9	10	20	30	40	50
VOLUME PER INJECTION	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	2.0	3.0	4.0	5.0*

* Limited data were collected on the administration >5.0 mL at a single injection site.

Preparation: IMMITICIDE should be aseptically reconstituted only with the provided 2 mL of STERILE DILUENT (sterile water for injection). Sterile water diluent is not suitable for intravascular injection. This provides 2.5 mg melsarsomine dihydrochloride per 0.1 mL of injectable solution. Two 50 mg vials will be required for dogs weighing >20 kg and 40 kg and 3 vials will be required for dogs >40 kg and 60 kg. Use immediately. Reconstituted solution may be used within 24 hours if refrigerated and kept from light.

Treatment Response: A baseline can be established pre-treatment by using commercially available in-office heartworm antigen test kits prior to treatment. Treatment response can be assessed best by heartworm antigen testing applied 4 months after treatment. A successful treatment is determined to be conversion from an antigen positive to an antigen negative status. In dogs with signs of heartworm disease, gradual improvement should be observed as the long-term effects of the heartworm infection resolve. Some dogs may have chronic effects that will not totally resolve.

CONCOMITANT THERAPY

During the course of clinical field trials, IMMITICIDE was administered concurrently with anti-inflammatories, antibiotics, insecticides, heartworm prophylactics, and various other drugs commonly used to stabilize and support dogs with heartworm disease with no adverse drug interactions noted.

Routine Prophylaxis: If the dog is not currently receiving commercially available heartworm preventatives, they may be administered consistent with label recommendations and re-exposure risk.

STORAGE CONDITIONS

Store upright at room temperature (15-25°C). After reconstitution, solutions should be stored under refrigeration and kept from light in the original packaging for 24 hours. Do not freeze reconstituted solution. No antimicrobial or other substance has been added to the sterile water diluent.

HOW SUPPLIED

IMMITICIDE is provided as:
5 - 50 mg vials of lyophilized melsarsomine dihydrochloride with accompanying 5 - 2 mL vials of sterile water for injection.

Marketed by
Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

Made in France.

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